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(71) Applicant: **American Cyanamid Company**
1937 West Main Street
Stamford Connecticut 06904(US)

(72) Inventor: **Grasso, Charles Paul**
15 Glen Oak Drive
East Windsor New Jersey 08520(US)

(74) Representative: **Diehl, Hermann O. Th., Dr. et al,**
Flüggenstrasse 17
D-8000 München 19(DE)

(54) **Process for the preparation of sulfur ylide intermediates of insecticidal pyrethroids.**

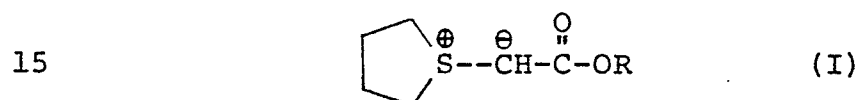
(57) The invention is an improved process for the preparation of lower alkyl esters of tetrahydrothiophenium carboxymethylide intermediates of insecticidal pyrethroids, and to insecticidal pyrethroids derived from said ylides.

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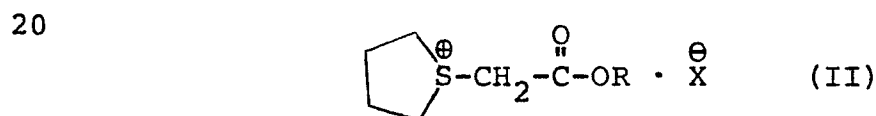
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AN IMPROVED PROCESS FOR THE PREPARATION OF
 10 SULFUR YLIDE INTERMEDIATES OF INSECTICIDAL PYRETHROIDS

The present invention relates to an improved process for the preparation of lower alkyl esters of tetrahydrothiophenium carboxymethylide of formula (I):



wherein R is C₁-C₄ alkyl, by a heterogeneous phase reaction comprising reacting a lower alkyl ester of a 1-(carboxymethyl)tetrahydrothiophenium halide salt of formula (II):



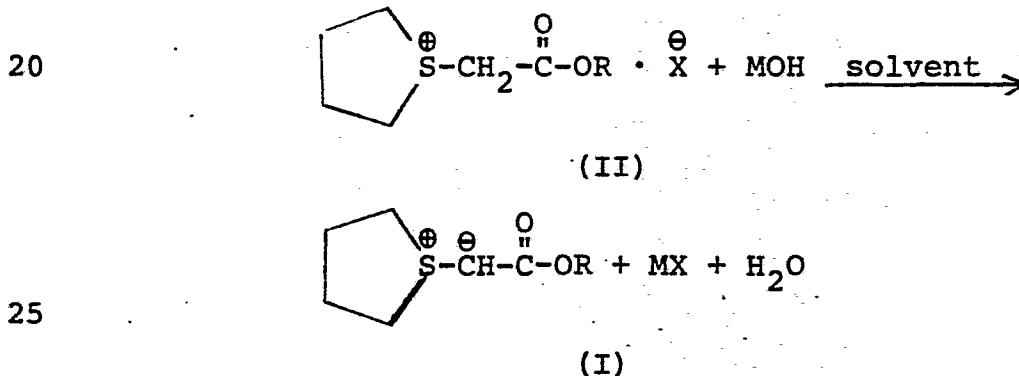
wherein R is as defined above and X is bromine or chlorine; with an anhydrous alkali metal hydroxide such as sodium or
 25 potassium hydroxide in the presence of an inert water immiscible solvent. On completion of the reaction, the insolubles present in the reaction mixture are mechanically separated from the solution of the formula (I) ylide. This solution may be used directly in subsequent reaction, or the yield
 30 may be isolated therefrom, if so desired.

The hereinabove briefly described process of the present invention has certain advantages when compared to known methods of the art utilized for the preparation of ylides, such as the process disclosed and claimed by W. W.
 35 Brand in U.S.P. 4,083,863 (issued 4/11/78) for the preparation of analogous tetrahydrothiophenium ylides and the pyrethroids prepared therefrom.

Notably, the by-products of the present process are solids, easily removable from the reaction mixture by mechanical means. Thus the problem of disposal of large amounts of highly alkaline effluents into the environment, and therefore contamination of same is avoided. Although at the present time effluents of the type described above and generated by the Brand process may be barged to sea and disposed there by dumping, this practice will be prohibited in the near future.

We also find that since the by-product of the present process is separated from the reaction as a solid mixture, wherein the components of the mixture comprise primarily alkali metal halide(s) and hydroxide(s), these may be easily and economically recovered from said mixture, if so desired.

Thus an "ylide" of formula (I) may be prepared by the process of the present invention as illustrated and described below:



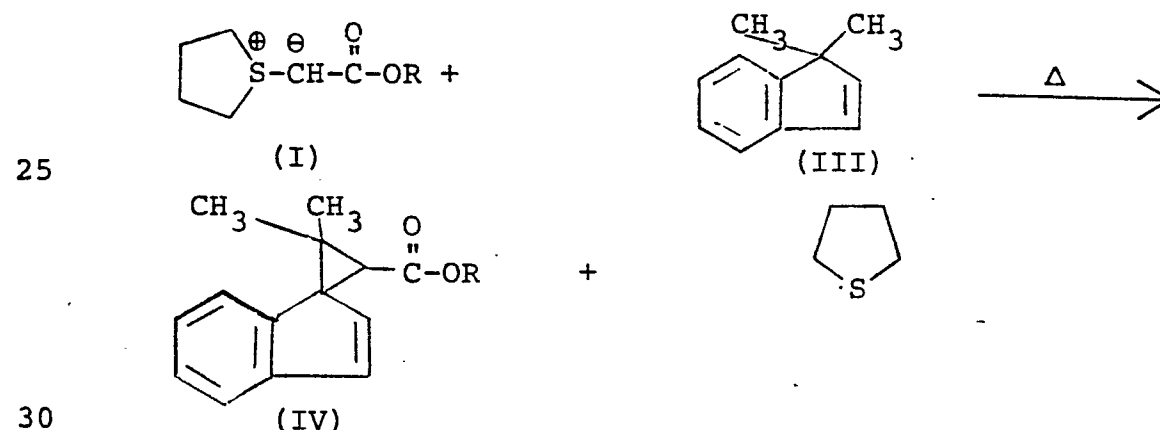
wherein R is C₁-C₄ alkyl, preferably ethyl; X is bromine or chlorine; M is sodium or potassium, preferably sodium.

Accordingly, a lower alkyl ester of a 1-(carboxymethyl)tetrahydrothiophenium halide of formula (II) is reacted with a solid, particulate alkali metal hydroxide of sodium or potassium hydroxide, preferably sodium hydroxide in a molar ratio of from about 1:1 to about 1:3 and preferably 1:2 to 1:3 in the presence of an inert water immiscible solvent of methylene chloride, chloroform, ethylene dichloride or mixtures thereof, in the temperature range of from

about 0°C to about 35°C and preferably 20 to 30°C for a period of time of from about one to five hours or until the reaction is essentially complete. The above heterogeneous phase reaction may be run under a blanket of inert dry gas such as nitrogen, if so desired, to prevent atmospheric moisture from entering the reaction vessel. The alkali metal hydroxide may be in the form of flakes, powder, pels or some other suitable particulate shape, although "pels" are preferred. On completion of the reaction, the mixture is filtered and the solution of the thus prepared ylide (I) may be used "as is" in the subsequent step leading to insecticidal pyrethroids, or said ylide may be isolated from the above solution if so desired.

It is recognized, that the use of excess anhydrous base also acts as a drying agent for the reaction system, hence there is less need to be concerned about the presence of small amounts of water in said reaction system, as is shown in Table I of Example 3.

Thus a cyclopropanecarboxylate of formula (IV), a key intermediate in the preparation of insecticidal pyrethroids, may be made from the ylide (I) as follows:



wherein R is as hereinabove defined.

In practice, about 0.9 to 1.0 molar equivalent of dimethylbenzofulvene (III) is added to the solution of the above ylide (I), the solvent is removed under vacuum at about 50°C to 60°C, and the residue heated under vacuum at 50°-60°C for a period of about 6 to 24 hours and preferably 6 to 8 hours until the reaction is essentially complete.

The tetrahydrothiophene is recovered by distillation at 90°C under vacuum, while the desired cyclopropanecarboxylate (IV) is recoverable from the reaction vessel.

The advantages and versatility of tetrahydrothio-
phenium ylides (I) in the preparation of cyclopropanecarboxylic acids, esters, and the insecticidal pyrethroids derived therefrom are well documented and illustrated in U.S.P. 4,083,863 (issued 4/11/78 to W. W. Brand; Assignee: American Cyanamid Company), and the information contained therein is
10 incorporated in the present application by way of reference.

The present invention is further illustrated by the following non-limiting examples.

EXAMPLE 1

Preparation of Tetrahydrothiophenium, Carboxymethylide, Ethyl
15 Ester.

Powdered potassium hydroxide (0.65 g; 0.01 mol) is added at room temperature to a vigorously stirred mixture of ethyl 1-(carboxymethyl)tetrahydrothiophenium bromide (2.5 g; 0.01 mol) and methylene chloride (20 ml). Stirring is con-
20 tinued for 15 minutes, the organic layer is then decanted and filtered. The solid residue from the reaction mixture is washed with methylene chloride (2 x 10 ml), the washings are decanted, filtered and combined with the above solution. The organic solution is concentrated at 40°C under vacuum,
25 and the residue held under vacuum at room temperature for 1/2 hour to afford 1.66 g (95%) of title product, a clear oil.

EXAMPLE 2

Preparation of the Ethyl Ester of 3,3-dimethylspiro[cyclo-
propane-1,1'-indene]-2-carboxylic acid.

30 Sodium hydroxide pels (44.0 g; 1.1 mol) are added to a stirred slurry of ethyl 1-(carboxymethyl)tetrahydrothiophenium bromide (187.0 g of 75% real; 0.55 mol) in methylene chloride (500 ml) at 18-20°C. The reaction mixture is stirred vigorously for 2 hours, is then filtered and the isolated
35 solids washed with methylene chloride (2 x 100 ml). The filtered solution and washings are combined and added to dimethylbenzofulvene (91.0 g of 85.7% pure; 0.5 mol). The

mixture is heated at 50°C and the solvent removed under vacuum in about 1.25 hours. The reaction mixture is then held under vacuum at 55°C for 22 hours and at room temperature for 36 hours. Analysis of a sample indicates the reaction mixture to contain 93% by weight of title product and 4.8% by weight of dimethylbenzofulvene. The latter is removed from the reaction mixture by heating same at 80°C under vacuum for 1.5 hours.

EXAMPLE 3

10 Evaluation of the effect of moisture, reaction time and the molar ratio of base to "sulfonium salt" on the formation of the corresponding "sulfonium ylide".

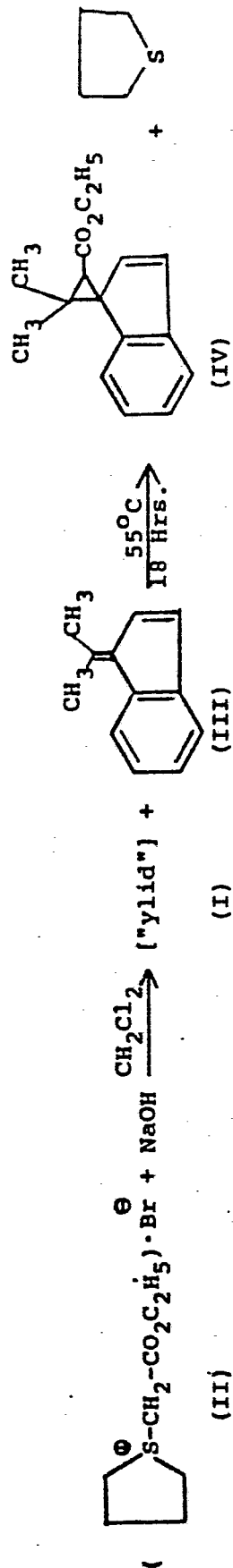
By the method of Example 2 a number of experiments are run in which the amount of sodium hydroxide pels is varied between 1.1 and 3 moles per mole of ethyl 1-(carboxymethyl)-tetrahydrothiophenium bromide. The reaction time is varied between 1.5 and 5 hours, while the methylene chloride used as reaction solvent is either anhydrous ("dry") or is saturated with water (at the temperature range the reaction is run).

The thus-formed ylide is then reacted with dimethylbenzofulvene at 55°C for a period of 18 hours by the procedure of Example 2, to afford the ethyl ester of 3,3-dimethylspiro[cyclopropane-1,1'-indene]-2-carboxylic acid. On completion of the reaction, the amount of product obtained is determined by gas chromatography (G.C.).

Pertinent data, including the results of G.C. analyses are compiled in Table I below, wherein it can be clearly seen that increased base concentrations have a major positive effect, the presence of water has a significant negative effect on the yields obtainable, while an almost equal positive interaction is noted between excess base and moisture content.

TABLE I

Reaction scheme:



Experiment	Molar Ratio NaOH: (II)	CH ₂ Cl ₂		Reaction time hours	Percent Yield of (IV)	Percent Recovery of (III)
		Dry	Saturated with H ₂ O			
1	1.1:1	+		3	60.9	36.2
2	1.1:1		+	3	45.9	49.0
3	1.1:1	+		1.5	70.6	27.3
4	1.1:1		+	1.5	44.2	46.3
5	2:1	+		3	87.7	10.4

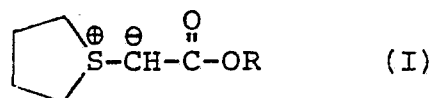
TABLE I (continued)

Experiment	Molar Ratio NaOH: (II)	CH ₂ Cl ₂		Reaction time hours	Percent Yield of (IV)	Percent Recovery Of (III)
		Dry	Saturated with H ₂ O			
6	2:1		+	3	85.8	12.5
7	2:1	+		1.5	85.3	13.7
8	2:1		+	1.5	86.6	12.0
9	2:1	*		5	87.0	11.8
10	3:1	*		2	90.6	8.6

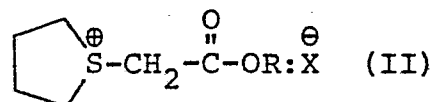
* = Standard reagent grade, not dried.

We claim:

1. A method for the preparation of a compound of formula:



wherein R is C₁-C₄ alkyl; comprising reacting a compound of formula:



wherein R is as hereinabove defined, and X is bromine or chlorine; with an equimolar to three molar amount of solid particulated alkali metal hydroxide of sodium hydroxide or potassium hydroxide in the presence of and dispersed in an inert water immiscible solvent in the temperature range of from 0°C to 35°C.

2. A method accord to Claim 1, wherein R is methyl or ethyl; the alkali metal hydroxide is sodium hydroxide used in 1.1:1 to 1:3 molar amount per mole of the compound of formula II of Claim 1; the water immiscible solvent is methylene chloride; and the temperature range is 20°C to 30°C.

3. A method according to Claim 2, wherein R is ethyl; X is bromine; the alkali metal hydroxide is sodium hydroxide used in 1:2 to 1:3 molar amount per mole of the compound of formula II; the solvent is methylene chloride, and the temperature range is 20°C to 30°C.



European Patent
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EUROPEAN SEARCH REPORT

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Application number

EP 80 10 3511

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl. ³)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
D	US - A - 4 083 863 (W.W. BRAND) * Column 6, lines 28-51; column 9, example 4, columns 11,12; example 14 * -----	1-3	C 07 D 333/46// C 07 C 69/74
			TECHNICAL FIELDS SEARCHED (Int. Cl.³)
			C 07 D 333/46
			CATEGORY OF CITED DOCUMENTS X: particularly relevant A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention E: conflicting application D: document cited in the application L: citation for other reasons
			&: member of the same patent family, corresponding document
☒ The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
The Hague		06-11-1980	CHOULY